

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicant : Cy A. Stein  
U.S. Serial No. : Not Yet Known (Continuation Application  
of PCT/US99/15250, filed 2 July 1999)  
Filed : Herewith  
For : OLIGONUCLEOTIDE INHIBITORS OF BCL-XL

1185 Avenue Of The Americas  
New York, New York 10036  
January 2, 2001

Assistant Commissioner for Patents  
Washington, D.C. 20231  
Box: Patent Application

Sir:

**PRELIMINARY AMENDMENT TO THE ACCOMPANYING CONTINUATION  
APPLICATION FILED UNDER 37 C.F.R. §1.53**

Applicants request that the following amendment be made in the  
above-identified application:

**In the Specification:**

On page 1, after the title, please delete the paragraph at lines  
3-5 beginning "This application is a continuation-in-part..." and  
insert the following as a separate paragraph:

--This application is a continuation of PCT International  
Application No. PCT/US99/15250, filed 2 July 1999,  
designating the United States of America, which is a  
continuation-in-part of U.S. Serial No. 09/109,614, filed  
July 2, 1998, the contents of which are hereby incorporated  
by reference into the present application.--

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**In the claims:**

Please cancel claims 1-4, 6-8, 10-16, 42, and 44-47 without disclaimer or prejudice to applicant's right to pursue the subject matter of these claims in a future continuation or divisional application.

Please amend claims 5, 9, 17, 27, 37 and 43 as follows:

--5. (Amended) [The] An antisense oligonucleotide [of claim 3,] comprising nucleotide sequence A, B, C, D, E, F, G, H, I, J, K, L, or M (SEQ ID NOS: 1-13), respectively, wherein the oligonucleotide is conjugated to a peptide.-

--9. (Amended) [The] An antisense oligonucleotide [of claim 3,] comprising nucleotide sequence A, B, C, D, E, F, G, H, I, J, K, L, or M (SEQ ID NOS: 1-13), respectively, wherein one or more of the oligonucleotide's sugars contain an -OMe group at their 2' position.--

--17. (Amended) A method of treating cancer, comprising introducing into a tumor cell an effective amount of [the] an antisense oligonucleotide [of claim 16,] comprising nucleotide sequence A, B, C, D, E, F, G, H, I, J, K, L, or M (SEQ ID NOS: 1-13), respectively, wherein the oligonucleotide comprises one or more bases with a C-5 propynyl pyrimidine modification, thereby reducing the levels of bcl-2 protein produced and treating cancer.-

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--27. (Amended) A method of treating cancer, comprising introducing into a tumor cell an effective amount of [the] an antisense oligonucleotide [of claim 3,] comprising nucleotide sequence A, B, C, D, E, F, G, H, I, J, K, L, or M (SEO ID NOS: 1-13), respectively, thereby reducing the levels of bcl-xL protein produced and treating cancer.--

--37. (Amended) A method of promoting the regression of vascular lesions, comprising introducing into a vascular cell an amount of [the] an antisense oligonucleotide [of claim 3] comprising nucleotide sequence A, B, C, D, E, F, G, H, I, J, K, L, or M (SEO ID NOS: 1-13), respectively, effective to reduce the levels of bcl-xL protein produced, thereby promoting the regression of vascular lesions.--

--43. (Amended) [The] A pharmaceutical composition [of claim 42,] comprising an effective amount of an antisense oligonucleotide or analog thereof of claim 3 and a pharmaceutically acceptable carrier, wherein the effective amount is between 0.1  $\mu$ M and 10  $\mu$ M.--

#### REMARKS

This application is a continuation of PCT International Application No. PCT/US99/15250, filed 2 July 1999, designating the United States of America, which is a continuation-in-part of U.S. Serial No. 09/109,614, filed July 2, 1998. Accordingly, the

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parent application, PCT International Application No. PCT/US99/15250, is pending today in the United States of America pursuant to 35 U.S.C. §363, and the subject continuation application is co-pending therewith in fulfillment of the provisions of 35 U.S.C. §120.

By this Preliminary Amendment, applicants have hereinabove amended the specification on page 1 to insert the continuation data. Applicants maintain that the amendments made hereinabove do not raise any issue of new matter. Accordingly, applicants respectfully request entry of the Amendment.

Claims 1-47 were pending in the subject application. By this Amendment, applicants have canceled claims 1-4, 6-8, 10-16, 42 and 44-47 without disclaimer or prejudice, and amended claims 5, 9, 17, 27, 37, and 43. Accordingly, upon entry of this Amendment, claims 5, 9, 17-41 and 43, as amended, will be pending.

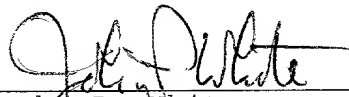
Support for the amendments to claims 5, 9, 17, 27, 37 and 43 may be found inter alia in the specification, as originally-filed, at page 13, line 35 through page 14, line 2 and page 15, lines 1-3; page 13, line 35 through page 14, line 2 and page 15, lines 13-16; page 13, line 35 through page 14, line 2 and page 16, lines 22-27; page 13, line 35 through page 14, line 2 and page 17, lines 7-8; page 13, line 35 through page 14, line 2 and page 18, line 25 through page 19, line 1; and page 13, line 35 through page 14, line 2, page 19, lines 15-18 and page 19, lines 9-10, respectively, and in originally filed claim 3 upon which these claims originally depended. Applicants, therefore, maintain that the amendments herein to the specification and the claims do not raise any issue of new matter and respectfully request that this Amendment be entered.

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If a telephone interview would be of assistance in advancing prosecution of the subject application, applicant's undersigned attorney invites the Examiner to telephone him at the number provided below.

No fee other than the filing fee of \$547.00, is deemed necessary in connection with this Preliminary Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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